? b 155
11jul03 14:49:06 User208669 Session D2339.1
$0.29 0.082 DialUnits File1
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File 155:MEDLINE(R) 1966-2003/Jul W1
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*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

Set Items Description
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Set Items Description
S1 1 VWF (W) CORE
S2 1031 CORE (W)PROMOTER
S3 6 WILLEBRAND AND S2
S4 1 MINIMAL AND PROMOTER AND (WILLEBRAND OR VWF)
S5 12 AU=GNATENKO?
? t s1/7
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DIALOG(R)File 155:MEDLINE(R)
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09489099 21265567 PMID: 11372677
The NFY transcription factor mediates induction of the von Willebrand factor promoter by irradiation.
Bertagna A; Jahroudi N
Department of Medicine, Albert Einstein College of Medicine, Bronx, NY 10461, USA.
Thrombosis and haemostasis (Germany) May 2001, 85 (5) p837-44, ISSN 0340-6245 Journal Code: 7608063
Contract/Grant No.: HL-54678; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Ionizing irradiation in patients is proposed to cause thrombus formation. An increase in von Willebrand factor secretion in response to irradiation is a major contributing factor to thrombus formation. We have previously reported that the increased VWF secretion in response to irradiation is mediated at the transcriptional level. The VWF core promoter fragment (sequences -90 to +22) was shown to contain the necessary cis-acting element(s) to mediate the irradiation response of the VWF gene. Here we report that a CCAAT element in the VWF promoter is the cis-acting element necessary for irradiation induction and that the NFY transcription factor interacts with this element. These analyses demonstrate that inhibition of NFY's interaction with the CCAAT element abolishes the irradiation induction of the VWF promoter. These results provide a novel role for NFY and add this factor to the small list of irradiation-responsive transcription factors. Coimmunoprecipitation experiments demonstrated that NFY is associated with the histone acetylase P/CAF in vivo and that irradiation resulted in an increased association of NFY with coactivator P/CAF. We propose that irradiation induction of the VWF promoter involves a mechanism resulting in increased recruitment of the coactivator P/CAF to the promoter via the NFY transcription factor.
Record Date Created: 20010524
Record Date Completed: 20020219
? t s3/7/1
3/7/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
11228433 98105702 PMID: 9444957
Ets transcription factors bind and transactivate the core promoter of the von Willebrand factor gene.
Schwachtgen J L; Janel N; Barek L; Duterque-Coquillaud M; Ghysdael J; Meyer D; Kerbiriou-Nabias D
INSERM U 143, Unite de Recherches sur l'Hemostase et la Thrombose, Hopital de Bicetre, France.
Oncogene (ENGLAND) Dec 18 1997, 15 (25) p3091-102, ISSN 0950-9232 Journal Code: 8711562
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
von Willebrand factor (vWF) gene expression is restricted to endothelial cells and megakaryocytes. Previous results demonstrated that basal transcription of the human vWF gene is mediated through a promoter located between base pairs -89 and +19 (cap site: +1) which is functional in endothelial and non endothelial cells. Two DNA repeats TTTCCTTT correlating with inverted consensus binding sites for the Ets family of transcription factors are present in the -56/-36 sequence. In order to analyse whether these DNA elements are involved in transcription, human umbilical vein endothelial cells (HUVEC), bovine calf pulmonary endothelial cell line (CPAE), HeLa and COS cells were transfected with constructs containing deletions of the -89/+19 fragment, linked to the chloramphenicol acetyl transferase (CAT) reporter gene. The -60/+19 region exhibits significant promoter activity in HUVEC and CPAE cells only. The -42/+19 fragment is not active. Mutations of the -60/+19 promoter fragment in the 5' (-56/-49) Ets binding site abolish transcription in endothelial cells whereas mutations in the 3' (-43/-36) site does not. The -60/-33 fragment forms three complexes with proteins from HUVEC nuclear extracts in electrophoretic

mobility shift assay which are dependent on the presence of the 5' Ets binding site. Binding of recombinant Ets-1 protein to the -60/-33 fragment gives a complex which also depends on the 5' site. The -60/+19 vWF gene core promoter is transactivated in HeLa cells by cotransfecting with Ets-1 or Erg (Ets-related gene) expression plasmids. In contrast to the wild type construct, transcription of the 5' site mutants is not increased by these expressed proteins. The results indicate that the promoter activity of the -60/+19 region of the vWF gene depends on transcription factors of the Ets family of which several members like Ets-1, Ets-2 and Erg are expressed in endothelium. Cotransfection of Ets-1 and Erg expression plasmids is sufficient to induce the -60/+19 vWF promoter activity in HeLa cells.

Record Date Created: 19980204

Record Date Completed: 19980204

? s minimal and promoter and (willebrand or vwf)

102104 MINIMAL

92108 PROMOTER

10841 WILLEBRAND

3808 VWF

S4 1 MINIMAL AND PROMOTER AND (WILLEBRAND OR VWF)

? t s4/7

4/7/1

DIALOG(R)File 155:MEDLINE(R)

08053374 94119118 PMID: 7507210

Endothelial-cell-specific regulation of von Willebrand factor gene expression.

Jahroudi N; Lynch D C

Department of Pathology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02115.

Molecular and cellular biology (UNITED STATES) Feb 1994, 14 (2) p999-1008, ISSN 0270-7306 Journal Code: 8109087

Contract/Grant No.: HL 33014; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

In both tissue sections and cell culture, the endothelial nature of a cell is most commonly determined by demonstration of its expression of von Willebrand factor (vWf) protein and/or mRNA. Thus, the mechanism of cell-type-specific transcriptional regulation of the vWf gene is central to studying the basis of endothelial-cell-specific gene expression. In this study, deletion analyses were carried out to identify the region of the vWf gene which regulates its endothelial-cell-specific expression. A 734-bp fragment which spans the sequence from -487 to +247 relative to the transcription start site was identified as the cell-type-specific promoter. It consists of a minimal core promoter located between -90 and +22, a strong negative regulatory element located upstream of the core promoter (ca. -500 to -300), and a positive regulatory region located downstream of the core promoter in the first exon. The activity of the core promoter is not cell type specific, and the negative regulatory region is required to inhibit its activity in all cell types. The positive regulatory region relieves this inhibition only in endothelial cells and results in endothelial-cell-specific gene expression. The positive regulatory region contains sequences predicting possible SP1, GATA, and octamer binding sites. Mutations in either the SP1 or octamer sequence have no effect on transcriptional activity, while mutation in the GATA binding element totally abolishes the promoter activity. Evidence that a GATA factor is involved in this interaction is presented. Thus, the positive regulatory region with an intact GATA binding site is required to overcome the inhibitory effect of the negative regulatory element and activate vWf gene expression in an endothelial-cell-specific manner.

Record Date Created: 19940224

Record Date Completed: 19940224

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5/7/3

DIALOG(R)File 155:MEDLINE(R)

11713717 99150035 PMID: 10027708

Human factor VIII can be packaged and functionally expressed in an adeno-associated virus background: applicability to haemophilia A gene therapy.

Gnatenko D V; Saenko E L; Jesty J; Cao L X; Hearing P; Bahou W F

Department of Medicine, State University of New York at Stony Brook 11794-8151, USA.

British journal of haematology (ENGLAND) Jan 1999, 104 (1) p27-36, ISSN 0007-1048 Journal Code: 0372544

Contract/Grant No.: AI41636; AI; NIAID; HL53665; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Adeno-associated virus (AAV) is a single-stranded DNA parvovirus displaying several attractive features applicable to haemophilia A gene therapy, including nonpathogenicity and potential for long-term transgene expression from either integrated or episomal forms. We have generated and characterized two B-domain-deleted (BDD) fVIII mutants, deleted in residues Phe756 to Ile1679 (fVIIIdelta756-1679) or Thr761 to Asn1639 (fVIIIdelta761-1639). [35S]metabolic labelling experiments and immunoprecipitation demonstrated intact BDD-fVIII of the predicted size in both lysates and supernatants (Mr approximately 155 kD for fVIIIdelta756-1679 and Mr approximately 160 kD for fVIIIdelta761-1639) after transient transfection into COS-1 cells. Functional fVIII quantification appeared maximal using fVIIIdelta761-1639, as evaluated by Coatest and clotting assay (98+/-20mU/ml/1x10(6) cells and 118+/-29

mU/ml/1x10(6) respectively, collection period 48 h). To bypass potential size limitations of rAAV/fVIII vectors, we expressed fVIIIdelta761-1639 using a minimal human 243 bp cellular small nuclear RNA (pHU1-1) promoter, and demonstrated VIII activity approximately 30% of that seen using CMV promoter. This BDD-fVIII (rAAV(pHU1-1) fVIIIdelta761-1639) can be efficiently encapsidated into rAAV (107% of wild type), as demonstrated by replication centre and DNAase sensitivity assays. A concentrated recombinant viral stock resulted in readily detectable factor VIII expression in COS-1 cells using a maximally-achievable MOI approximately 35 (Coatest 15 mU/ml; clotting assay 25+/-20 mU/ml/1x10(6) cells). These data provide the first evidence that rAAV is an adaptable virus for fVIII delivery, and given the recent progress using this virus for factor IX delivery in vivo, provide a new approach towards definitive treatment of haemophilia A.

Record Date Created: 19990322

Record Date Completed: 19990322

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DIALOG(R)File 155:MEDLINE(R)

10886415 97238259 PMID: 9084579

Characterization of recombinant adeno-associated virus-2 as a vehicle for gene delivery and expression into vascular cells.

Gnatenko D; Arnold T E; Zolotukhin S; Nuovo G J; Muzyczka N; Bahou W F

Department of Medicine, State University of New York at Stony Brook 11794-8151, USA.

Journal of investigative medicine - the official publication of the American Federation for Clinical Research (UNITED STATES) Feb 1997, 45 (2) p87-98, ISSN 1081-5589 Journal Code: 9501229

Contract/Grant No.: HL49141; HL; NHLBI; HL50257; HL; NHLBI; HL53665; HL; NHLBI; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: We have used wild-type and recombinant adeno-associated virus-2 (AAV) to study transduction, replication efficiencies, functional protein expression, and gene delivery to vascular cells in vitro and in vivo. METHODS: Recombinant adeno-associated virus-2 (rAAV) plasmids (ranging in size to 110% of wild-type AAV) driven by 6 distinct promoters upstream of a beta-galactosidase cassette were effectively used for generation of replication-deficient virus, with titers consistently ranging from 2.5 x 10(5) IU/mL. AAV infectivity and replication in human umbilical vein endothelial cells (HUVEC) were unrelated to cellular proliferative index establishing the potential utility of the virus for transduction of quiescent vascular cells. Long-term cultures of AAV-infected HUVEC established the presence of episomal forms at 18 days, although chromosome 19-specific integration was not evident. Functional beta-galactosidase activity approximately 400% above control was evident in HUVEC using either a murine collagen alpha 1(I) promoter (pTRCol alpha 1(I) beta) or CMV promoter (pTRCMV beta). RESULTS: Based on these initial data, in vivo studies were completed using a rat carotid artery model. Both wild-type AAV (titers -1X10(9) IU/mL) and rAAV (pTRCol alpha 1(I) beta or pTRCMV beta) efficiently infected vascular cells in vivo with endothelial and vascular smooth muscle cell transduction frequencies approaching 90% as judged by DNA in situ polymerase chain reaction, with no evidence for disrupted vessel architecture. Protein expression using total vessel extracts at 48 hours postinfection demonstrated 20-fold increase in functional beta-galactosidase activity using pTRCol alpha 1(I) beta compared to saline-injected controls vessels (799 +/- 236 microU/mg protein vs 40.7 +/- 17 microU/mg protein). CONCLUSIONS: These data provide the first evidence that rAAV may be adapted for directed high-level transgene delivery and expression into normally quiescent vascular endothelial and smooth muscle cells both in vitro and in vivo.

Record Date Created: 19970428

Record Date Completed: 19970428

? log hold

11jul03 15:06:29 User208669 Session D2339.2

$3.35 1.048 DialUnits File155

$0.00 18 Type(s) in Format 6

$1.05 5 Type(s) in Format 7

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$4.40 Estimated cost File155

$4.20 TELNET

$8.60 Estimated cost this search

$8.90 Estimated total session cost 1.130 DialUnits

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